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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,493	06/08/2007	Takahide Kohro	032218A	1082

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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
04/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,493	KOHRO ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/30/2008* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/2006 and 8/24/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group V in the reply filed on 12/30/2008 is acknowledged. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/30/2008.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. **Claims 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

6. Instant claim 13 is drawn to a "method of screening a blood vessel remedy". It is unclear from the claim as recited, and the specification does not provide adequate guidance, for one of ordinary skill in the art to ascertain the meaning of "a blood vessel remedy". As defined by the *Merriam-Webster Online Dictionary*, a remedy is (1) a medicine, application, or treatment that relieves or cures a disease or (2) something that

corrects or counteracts. Since a blood vessel is not a disease to be relieved or cured, the second definition (but not the first definition) is applied to the instant claims. In view of this definition, a "blood vessel remedy" could be interpreted as something that **corrects** blood vessels or (for example, by treating a blood vessel condition or disorder such as atherosclerosi), alternatively, something that **counteracts** blood vessels (for example, by inhibiting angiogenesis in the treatment of cancer). Since it is unclear which meaning of "blood vessel remedy" applies to the instant claims, it would be impossible for the skilled artisan to recognize the metes and bounds of the claim. As such, the phrase "blood vessel remedy" renders instant claim 13 indefinite. Dependent claims 14-15, which fail to clarify the meaning of "blood vessel remedy" are also rejected as indefinite.

7. **Claims 13-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for screening a blood vessel remedy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.**

8. Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered, with the most relevant factors discussed below.

9. **Nature of the invention**: The instant invention is drawn to a method of screening a blood vessel remedy, which comprises adding a test substance to a Rac protein-expressing cell and measuring the transfer of Rac protein into the nucleus (claim 13), more specifically wherein the Rac protein is in the form of a fusion protein with a fluorescent protein (claim 14) and/or wherein the transfer of Rac protein into the nucleus is measured by observation with fluorescence (claim 15). As discussed above, the phrase "blood vessel remedy" is indefinite. However, for purposes of examination, the phrase "blood vessel remedy" is understood to encompass a substance that is capable of treating a vascular disease or condition such as atherosclerosis. As such, the nature of the invention is complex.

10. **Breadth of the claims**: The claims are broad in that they encompass a method for screening a substance for treating a vascular disease or condition (such as atherosclerosis) by adding a test substance to a Rac protein-expressing cell and measuring the transfer of Rac protein into the nucleus. As such, the claims are extremely broad in that **any** test substance can be added and screened for its ability to treat **any** vascular disease or condition. Furthermore, the claims are broad in that the method involves measuring the transfer of Rac protein into the nucleus but does not specify the amount of Rac protein transfer to the nucleus that must be measured to indicate that the test compound is capable of being used as a "blood vessel remedy" or the period of time over which the Rac protein-expressing cell should be monitored for Rac transfer. Thus, the breadth of the claims is extreme broad, which further exacerbates the complexity of the invention.

11. **Guidance of the specification/The existence of working examples**: The amount of direction provided by the Applicant is considered to be determined by the specification and the working examples. In the instant case, Applicant has provided data which allegedly indicate that Rac protein is transported into the nucleus of HUVECs (Page 14) following treatment with pitavastatin which, as taught by *Masamura et al* (Ateriosclerosis Thromb Vasc Biol 23:512-517, 2003), is an HMG CoA reductase inhibitor useful for the treatment of vascular conditions and disorders (Abstract). However, Applicant's data do **not** demonstrate that the observed translocation of Rac into the nucleus is in any way responsible for pitavastatin's therapeutic effects. That is, there is nothing to suggest that the transfer of Rac into the nucleus is necessary for a substance (such as pitavastatin) to function as a blood vessel remedy. For example, Applicant does not demonstrate that blocking the transfer of Rac into the nucleus blocks the protective effects of pitavastatin so as to indicate that nuclear import of Rac is necessary for pitavastatin's therapeutic effects. Accordingly, it is unclear whether adding a test substance to a Rac protein expressing cell and measuring the transfer of Rac protein into the nucleus would in any way indicate that the test substance is capable of being used as a blood vessel remedy as recited by instant claims. Furthermore, even assuming *arguendo* that the ability of a test substance to promote Rac protein transfer to the nucleus did indicate that the test substance could be used as a "blood vessel remedy", the specification does not provide guidance as to the amount of Rac protein which must be transfered into the nucleus. That is, the skilled artisan would not be able to determine (based on Applicant's specification) whether a test

substance that increases nuclear Rac levels by 0.00001% (based on increased fluorescence) would be capable of being used as a blood vessel remedy, or whether more Rac protein must be transferred into the nucleus for the test substance to be effective. Additionally, Applicant does not disclose the period of time over which nuclear transport of Rac should be monitored (minutes/days/weeks/months/years).

12. **State of the art/Predictability of the art**: The level of predictability in the art is considered to be relatively low.

13. **Amount of experimentation necessary**: Given the complex nature of the invention, which is exacerbated by the breadth of the claims, and given the lack of working examples and the high degree of unpredictability in the art, it would require undue experimentation for a person of ordinary skill in the art to use the invention as claimed. Since any compound that promotes any transfer of Rac protein into the nucleus over any period of time would qualify as an agent capable of treating any condition of the vasculature according to the instant method (and further, considering there is no demonstrated connection between Rac nuclear transport and activity as a blood vessel remedy), it would require undue experimentation to identify which of the test compounds are actually capable of being used as a blood vessel remedy.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614